(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 29 April 2004 (29.04.2004)

(10) International Publication Number WO 2004/034789 A1

- (51) International Patent Classification7: A01N 63/00, C07H 21/02, 21/04, C12N 15/00, 15/63, C12P 21/06
- (21) International Application Number:

PCT/US2002/033243

- (22) International Filing Date: 15 October 2002 (15.10.2002)
- (25) Filing Language:

English

(26) Publication Language:

English

- (71) Applicant (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES OF AMERICA represented BY THE SECRETARY DE-PARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; National Institutes of Health, Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): LIU, Ke [US/US]; 14 Sweetwood Court, Rockville, MD 20850 (US). ROSEN-BERG, Steven, A. [US/US]; 10104 Iron Gate Road, Potomac, MD 20854 (US).
- (74) Agents: LARCHER, Carol et al.; Leydig, Voit & Mayer, LTD., Two Prudential Plaza, Suite 4900, 180 N. Stetson, Chicago, IL 60601-6780 (US).

- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

as to non-prejudicial disclosures or exceptions to lack of novelty (Rule 4.17(v)) for the following designation JP

Published:

- with international search report
- with a declaration as to non-prejudicial disclosures or exceptions to lack of novelty

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS OF PREPARING LYMPHOCYTES THAT EXPRESS INTERLEUKIN-2 AND THEIR USE IN THE TREATMENT OF CANCER

2004/034789 (57) Abstract: A method of preparing autologus T-lymphocytes for re-introduction into a patient having cancer, which method comprises obtaining peripheral blood mononuclear cells (PBMCs) from a patient immunized with an antigen of the canneer, stimulating the PBMCs with the antigen of the cancer in vitro, transducing the PBMCs with a retrovial vector, which (a) comprises and expresses a human interleukin-2 (IL-2) coding sequence operably linked to a retroviral promoter, (b) does not comprise an exogenously introduced gene that enables phenotypic selection, and (c) comprises a viral envelope that efficiently transduces CD8+ T-lymphocytes; a method of preparing autologous tumor-infiltrating lymphocytes (TILs) for reintroduction into a patient having cancer, which method comprises obtaining TILs from a tumor of the patient, optionally immunized with an antigen of the cancer, optionally stimulating the TILs with the antigen of the cancer in vitro, and transducing the TILs with the aforementioned retroviral vector; compositions comprising cells obtained in accordance with such methods; and methods of treating a patient having cancer by administering to the patient cells obtained in accordance with such methods or compositions comprising same.

